

REMARKS

Claims 1-5 have been amended and claims 6 and 7 withdrawn from consideration. At item 4 a) of the Office Action Summary, it is incorrectly stated that claims 7 and 8 have been withdrawn from consideration. It is respectfully requested that this entry be amended to properly read claims 6 and 7, which have been withdrawn as a result of the restriction requirement of January 3, 2006.

Claims 1-4 have been amended to convert "use" claims into "process" claims.

Newly amended claims 1 and 5 recite aspects of the invention and are fully supported by the specification. For example, hydrolysis of phosphoester (P-O) bonds is disclosed at page 4, lines 15-20 of the instant specification. The substrates that are suitable for the claimed phosphomidase assay are disclosed page 6, lines 15-19 of the instant specification. No new matter is added.

Rejection Under 35 U.S.C. §112, first paragraph

The use claims are rewritten to be in acceptable US claim language format.

Accordingly, it is courteously requested that the rejection of claims 1-4 under 35 U.S.C. §112 be withdrawn.

Rejection Under 35 U.S.C. §102 (b)

The rejection of claims 1-4, 8, and 9 under 35 U.S.C. §102 (b) as being anticipated by Mountfort et al. (*Toxicon*, **37**, pages 909-922, **1999**) is respectfully traversed.

At the outset, Applicants would like to distinguish between the protein phosphatase of the cited reference and the phosphoamidase of the instant invention. The description of the present application and the prior art cited in the present invention (Ek,P. et al., *Eur. J. Biochem.* **269**, 5016-5023, **2002**) defines phosphoamidase as "an enzyme hydrolyzing phosphoamide (P-N) bonds...and which is devoid of an activity that hydrolyzes O-phosphorylated proteins or peptides" (see page 3, lines 27-34 of the instant specification). It is obvious from the specification that the phosphoamidases are enzymes that are capable of metabolizing phospho-amide (P-N) bonds of N-phosphorylated amino acid substrates (see page 1, lines 10-16 of the instant specification). In contrast, protein phosphatases are

biochemically characterized as having intrinsic hydrolyzing activity against phosphate monoester bonds (P-O) bonds. The relevant distinction is also made by the International Union of Biochemistry and Molecular Biology (IUBMB) enzyme nomenclature system.

Mountfort et al. discloses a fluorescence assay for measuring the inhibition of protein phosphatase by okadaic acid (see Abstract). Nothing suggests that phosphoamidase (an enzyme defined as not cleaving P-O bonds in peptides and proteins, as does a phosphatase such as that of Mountfort could cleave the P-O bonds in the particular, non-peptidic substrates recited in the claims. This is totally unexpected.

Since, all material elements of the claims are not disclosed in the cited reference, the teachings of Mountfort cannot anticipate the phosphoamidase assay claimed by the instant invention. Hence, proper withdrawal of the pending rejection is respectfully requested.

Rejection Under 35 U.S.C. § 103 (a)

The rejection of claims 1-5 and 8-10 under 35 U.S.C. § 103 (a) as being unpatentable over Mountfort et al. in view of Klumpp et al. (US 6,812,015) and further in view of Kim et al. (*Journal of Biological Chemistry*, **268**, pages 18513-18518, **1993**) is respectfully traversed.

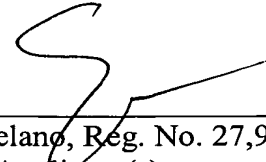
The various deficiencies of the primary reference of Mountfort et al. should render the obviousness rejections moot. However, the following comments on the references are provided for competence.

The secondary references of Klumpp and Kim, along with the cited reference (Molecular Probes, Citation No. 2) are directed to protein phosphatases and a method of measuring the activity of such phosphatases based on the hydrolysis of a phosphate monoester (P-O) bond (see Fig. 2 of Klumpp et al. and *Phosphatase Assay* under Materials and Methods of Kim et al.). More specifically, histidine protein phosphatases of both Klumpp and Kim are protein phosphatases. See claims 1, 7, and 8 of Klumpp et al and Fig. 1, 2, 6, and 7 of Kim et al. There is nothing in the teaching of either the primary or secondary reference so as to suggest to one of ordinary skill in the art to use the claimed substrates in measuring the *phosphomidase activity* of the claimed proteins. The assay methods disclosed by Klumpp and Kim are directed to the hydrolysis of phosphate monoester (P-O) bonds, they do not reveal any information about the hydrolysis of phospho-amide (P-N) bonds.

Accordingly, it is respectfully requested that the rejection be withdrawn.

No fee is believed to be due with this response, however, the Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



Anthony J. Zelano, Reg. No. 27,969
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
Arlington Courthouse Plaza 1
2200 Clarendon Boulevard, Suite 1400
Arlington, VA 22201
Direct Dial: 703-812-5311
Facsimile: 703-243-6410
Attorney Docket No.: MERCK-2907
Date: May 30, 2006